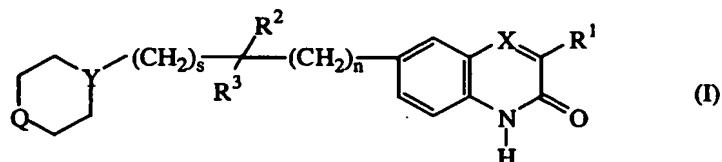


CLAIMS

1. A compound of formula (I),



5

the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

10 n is 0 or 1;

s is 0 or 1;

X is $-N=$ or $-CR^4=$, wherein R^4 is hydrogen or taken together with R^1 may form a bivalent radical of formula $-CH=CH-CH=CH-$;

15

Y is $-N<$ or $-CH<$;

Q is $-NH-$, $-O-$, $-C(O)-$, $-CH_2-CH_2-$ or $-CHR^5-$,

wherein R^5 is hydrogen, hydroxy, C_{1-6} alkyl, aryl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl,

20 C_{1-6} alkyloxy C_{1-6} alkylamino or haloindazolyl;

R^1 is C_{1-6} alkyl or thienyl;

R^2 is hydrogen or taken together with R^3 may form $=O$;

25

R^3 is hydrogen, C_{1-6} alkyl or a radical selected from

- NR^6R^7 (a-1),

- $O-H$ (a-2),

- $O-R^8$ (a-3),

30 - $S-R^9$ (a-4), or

— $C\equiv N$ (a-5),

wherein

R^6 is $-CHO$, C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyl, di(C_{1-6} alkyl)amino C_{1-6} alkyl, C_{1-6} alkylcarbonylamino C_{1-6} alkyl,

piperidinylC₁₋₆alkyl, piperidinylC₁₋₆alkylaminocarbonyl, C₁₋₆alkyloxy, C₁₋₆alkyloxyC₁₋₆alkyl, thienylC₁₋₆alkyl, pyrrolylC₁₋₆alkyl, arylC₁₋₆alkylpiperidinyl, arylcarbonylC₁₋₆alkyl, arylcarbonylpiperidinylC₁₋₆alkyl, haloindozolylpiperidinylC₁₋₆alkyl, or arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl; and R⁷ is hydrogen or C₁₋₆alkyl;

5

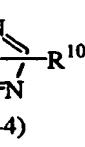
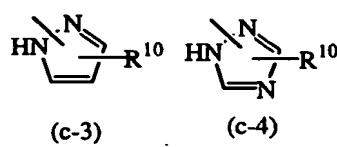
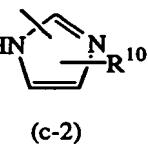
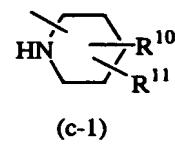
R⁸ is C₁₋₆alkyl, C₁₋₆alkylcarbonyl or di(C₁₋₆alkyl)aminoC₁₋₆alkyl; andR⁹ is di(C₁₋₆alkyl)aminoC₁₋₆alkyl;or R³ is a group of formula-(CH₂)_t-Z- (b-1),

10

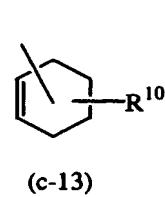
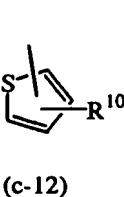
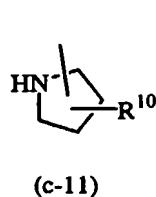
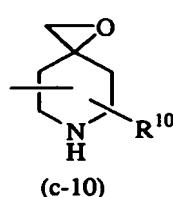
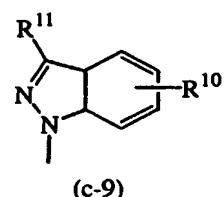
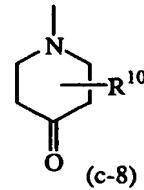
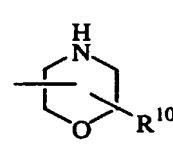
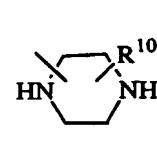
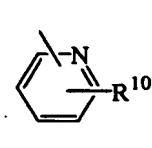
wherein

t is 0, 1 or 2;

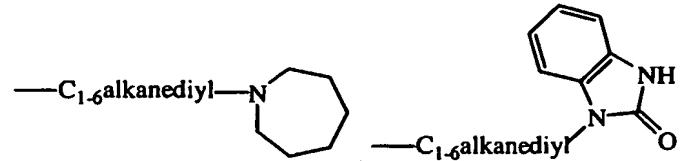
Z is a heterocyclic ring system selected from



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20

wherein each R¹⁰ independently is hydrogen, C₁₋₆alkyl, aminocarbonyl, hydroxy,

C₁₋₆alkyloxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkylamino, di(phenylC₂₋₆alkenyl), piperidinylC₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkylC₁₋₆alkyl, aryloxy(hydroxy)C₁₋₆alkyl, haloindazolyl, arylC₁₋₆alkyl, arylC₂₋₆alkenyl, morpholino, C₁₋₆alkylimidazolyl, or pyridinylC₁₋₆alkylamino;

25

each R¹¹ independently is hydrogen, hydroxy, piperidinyl or aryl;

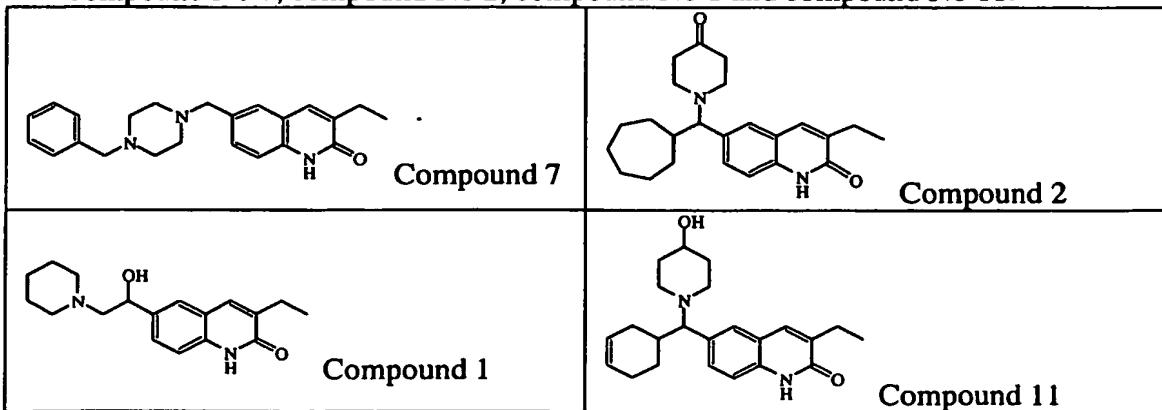
aryl is phenyl or phenyl substituted with halo, C₁₋₆alkyl or C₁₋₆alkyloxy;

5 with the proviso that 6-(cyclohexyl-1*H*-imidazol-1-ylmethyl)-3-methyl-2(1*H*)-quinoxalinone is not included.

10 2. A compound as claimed in claim 1 wherein X is -N= or -CH=; R¹ is C₁₋₆alkyl; R³ is hydrogen, C₁₋₆alkyl, a radical selected from (a-1), (a-2), (a-3) or (a-4) or a group of formula (b-1); R⁶ is di(C₁₋₆alkyl)aminoC₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl; R⁷ is hydrogen; R⁸ is di(C₁₋₆alkyl)aminoC₁₋₆alkyl; t is 0 or 2; Z is a heterocyclic ring system selected from (c-1), (c-5), (c-6), (c-8), (c-10), (c-12) or (c-13); each R¹⁰ independently is hydrogen, C₁₋₆alkyl, hydroxy, C₁₋₆alkyloxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkylamino, morpholino, C₁₋₆alkylimidazolyl, or pyridinylC₁₋₆alkylamino; each R¹¹ independently is hydrogen or hydroxy; and aryl is phenyl.

15 3. A compound according to claim 1 and 2 wherein n is 0; X is CH; Q is -NH-, -CH₂-CH₂- or -CHR⁵-, wherein R⁵ is hydrogen, hydroxy, or arylC₁₋₆alkyl; R¹ is C₁₋₆alkyl; R² is hydrogen; R³ is hydrogen, hydroxy or a group of formula (b-1); t is 0; Z is a heterocyclic ring system selected from (c-8) or (c-13); each R¹⁰ independently is hydrogen; and aryl is phenyl.

20 4. A compound according to claim 1, 2 and 3 wherein the compound is selected from compound No 7, compound No 2, compound No 1 and compound No 11.

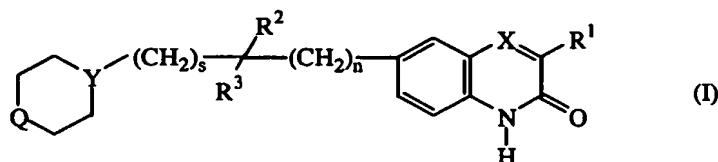


25 5. A compound as claimed in any of claims 1 to 4 for use as a medicine.

6. A pharmaceutical composition comprising pharmaceutically acceptable carriers and as an active ingredient a therapeutically effective amount of a compound as claimed in claim 1 to 4.

5 7. A process of preparing a pharmaceutical composition as claimed in claim 6 wherein the pharmaceutically acceptable carriers and a compound as claimed in claim 1 to 4 are intimately mixed.

10 8. Use of a compound for the manufacture of a medicament for the treatment of a PARP mediated disorder, wherein the compound is a compound of formula (I)



15 the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereo-chemically isomeric forms thereof, wherein

n is 0 or 1;

s is 0 or 1;

20 X is -N= or -CR⁴=, wherein R⁴ is hydrogen or taken together with R¹ may form a bivalent radical of formula -CH=CH-CH=CH-;

Y is -N< or -CH<;

25 Q is -NH-, -O-, -C(O)-, -CH₂-CH₂- or -CHR⁵-,
wherein R⁵ is hydrogen, hydroxy, C₁₋₆alkyl, arylC₁₋₆alkyl, C₁₋₆alkyloxycarbonyl,
C₁₋₆alkyloxyC₁₋₆alkylamino or haloindazolyl;

30 R¹ is C₁₋₆alkyl or thienyl;

R² is hydrogen or taken together with R³ may form =O;

R³ is hydrogen, C₁₋₆alkyl or a radical selected from

5

- NR⁶R⁷ (a-1),
- O-H (a-2),
- O-R⁸ (a-3),
- S- R⁹ (a-4), or
- C≡N (a-5),

wherein

R⁶ is -CHO, C₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyl, di(C₁₋₆alkyl)aminoC₁₋₆alkyl, C₁₋₆alkylcarbonylaminoC₁₋₆alkyl, piperidinylC₁₋₆alkyl, piperidinylC₁₋₆alkylaminocarbonyl, C₁₋₆alkyloxy, C₁₋₆alkyloxyC₁₋₆alkyl, thienylC₁₋₆alkyl, pyrrolylC₁₋₆alkyl, arylC₁₋₆alkylpiperidinyl, arylcarbonylC₁₋₆alkyl, arylcarbonylpiperidinylC₁₋₆alkyl, haloindozolylpiperidinylC₁₋₆alkyl, or arylC₁₋₆alkyl(C₁₋₆alkyl)aminoC₁₋₆alkyl; and R⁷ is hydrogen or C₁₋₆alkyl;

10 R⁸ is C₁₋₆alkyl, C₁₋₆alkylcarbonyl or di(C₁₋₆alkyl)aminoC₁₋₆alkyl; and R⁹ is di(C₁₋₆alkyl)aminoC₁₋₆alkyl;

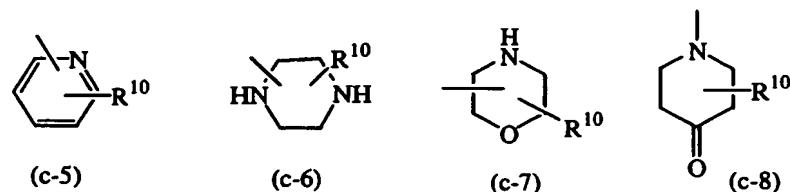
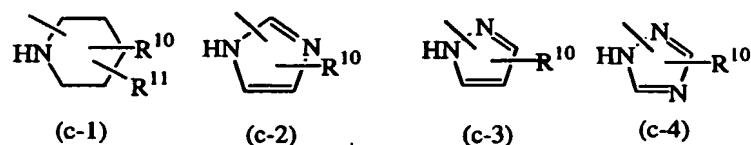
15 or R³ is a group of formula

- (CH₂)_t-Z- (b-1),

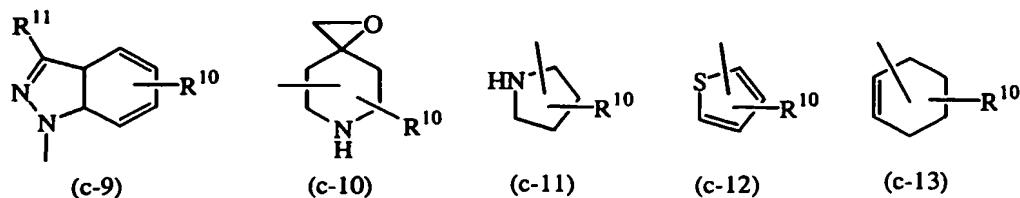
wherein

t is 0, 1 or 2;

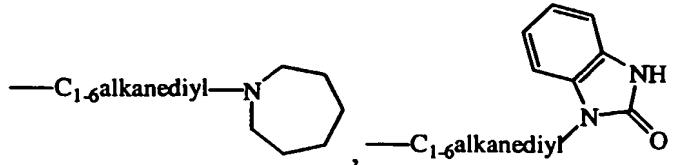
20 Z is a heterocyclic ring system selected from



25



wherein each R¹⁰ independently is hydrogen, C₁₋₆alkyl, aminocarbonyl, hydroxy,



C₁₋₆alkyloxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkylamino, di(phenylC₂₋₆alkenyl), piperidinylC₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkylC₁₋₆alkyl,

5 aryloxy(hydroxy)C₁₋₆alkyl, haloindazolyl, arylC₁₋₆alkyl, arylC₂₋₆alkenyl, morpholino, C₁₋₆alkylimidazolyl, or pyridinylC₁₋₆alkylamino; each R¹¹ independently is hydrogen, hydroxy, piperidinyl or aryl;

aryl is phenyl or phenyl substituted with halo, C₁₋₆alkyl or C₁₋₆alkyloxy.

10

9. Use according to claim 8 of a PARP inhibitor of formula (I) for the manufacture of a medicament for the treatment of a PARP-1 mediated disorder

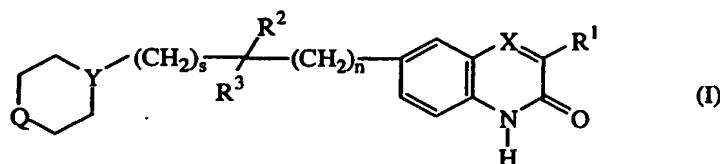
10. Use according to claim 8 and 9 wherein the treatment involves chemosensitization.

15

11. Use according to claims 8 and 9 wherein the treatment involves radiosensitization.

12. A combination of a compound with a chemotherapeutic agent wherein said compound is a compound of formula (I)

20



the N-oxide forms, the pharmaceutically acceptable addition salts and the stereo-chemically isomeric forms thereof, wherein

25

n is 0 or 1;

s is 0 or 1;

X is -N= or -CR⁴=, wherein R⁴ is hydrogen or taken together with R¹ may form a

30 bivalent radical of formula -CH=CH-CH=CH-;

Y is $-N<$ or $-CH<;$

Q is $-NH-$, $-O-$, $-C(O)-$, $-CH_2-CH_2-$ or $-CHR^5-$,

wherein R^5 is hydrogen, hydroxy, C_{1-6} alkyl, aryl C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl,

5 C_{1-6} alkyloxy C_{1-6} alkylamino or haloindazolyl;

R^1 is C_{1-6} alkyl or thienyl;

R^2 is hydrogen or taken together with R^3 may form $=O$;

10

R^3 is hydrogen, C_{1-6} alkyl or a radical selected from

- NR^6R^7 (a-1),

- $O-H$ (a-2),

- $O-R^8$ (a-3),

15 - $S-R^9$ (a-4), or

— $C\equiv N$ (a-5),

wherein

R^6 is $-CHO$, C_{1-6} alkyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyl,

di(C_{1-6} alkyl)amino C_{1-6} alkyl, C_{1-6} alkylcarbonylamino C_{1-6} alkyl,

20

piperidinyl C_{1-6} alkyl, piperidinyl C_{1-6} alkylaminocarbonyl, C_{1-6} alkyloxy,

C_{1-6} alkyloxy C_{1-6} alkyl, thieryl C_{1-6} alkyl, pyrrolyl C_{1-6} alkyl,

aryl C_{1-6} alkylpiperidinyl, arylcarbonyl C_{1-6} alkyl, arylcarbonylpiperidinyl C_{1-6} alkyl,

haloindozolylpiperidinyl C_{1-6} alkyl, or aryl C_{1-6} alkyl(C_{1-6} alkyl)amino C_{1-6} alkyl; and

R^7 is hydrogen or C_{1-6} alkyl;

25

R^8 is C_{1-6} alkyl, C_{1-6} alkylcarbonyl or di(C_{1-6} alkyl)amino C_{1-6} alkyl; and

R^9 is di(C_{1-6} alkyl)amino C_{1-6} alkyl;

or R^3 is a group of formula

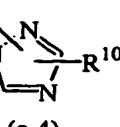
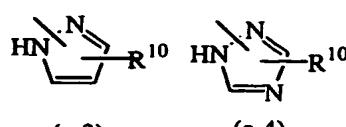
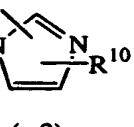
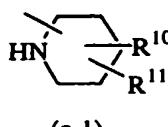
- $(CH_2)_t-Z-$ (b-1),

wherein

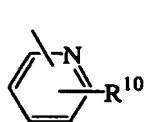
30

t is 0, 1 or 2;

Z is a heterocyclic ring system selected from



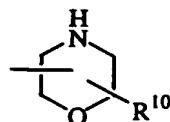
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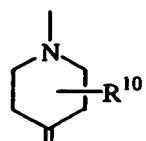
(c-5)



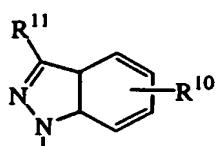
(c-6)



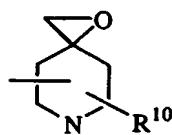
(c-7)



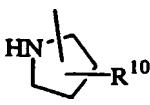
(c-8)



(c-9)



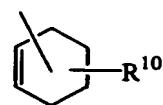
(c-10)



(c-11)

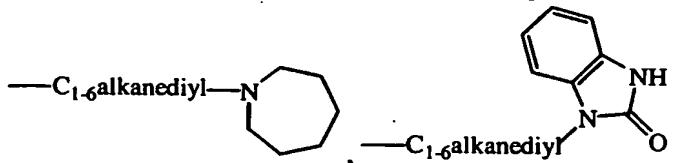


(c-12)



(c-13)

5 wherein each R¹⁰ independently is hydrogen, C₁₋₆alkyl, aminocarbonyl, hydroxy,



C₁₋₆alkyloxyC₁₋₆alkyl, C₁₋₆alkyloxyC₁₋₆alkylamino, di(phenylC₂₋₆alkenyl), piperidinylC₁₋₆alkyl, C₃₋₁₀cycloalkyl, C₃₋₁₀cycloalkylC₁₋₆alkyl, aryloxy(hydroxy)C₁₋₆alkyl, haloindazolyl, arylC₁₋₆alkyl, arylC₂₋₆alkenyl, morpholino, C₁₋₆alkylimidazolyl, or pyridinylC₁₋₆alkylamino;

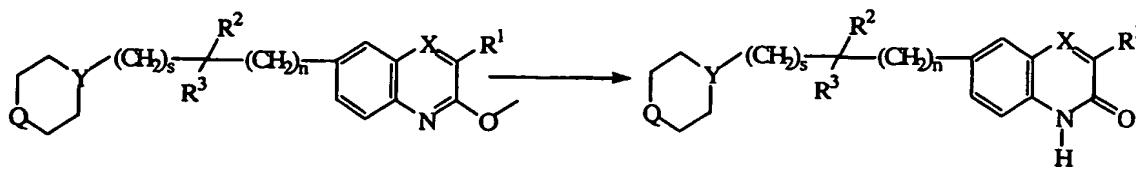
10 each R¹¹ independently is hydrogen, hydroxy, piperidinyl or aryl;

aryl is phenyl or phenyl substituted with halo, C₁₋₆alkyl or C₁₋₆alkyloxy.

15 13. A process for preparing a compound as claimed in claim 1, characterized by

a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents, such as, tinchloride, acetic acid and hydrochloric acid, in the presence of a reaction inert solvent, e.g. tetrahydrofuran.

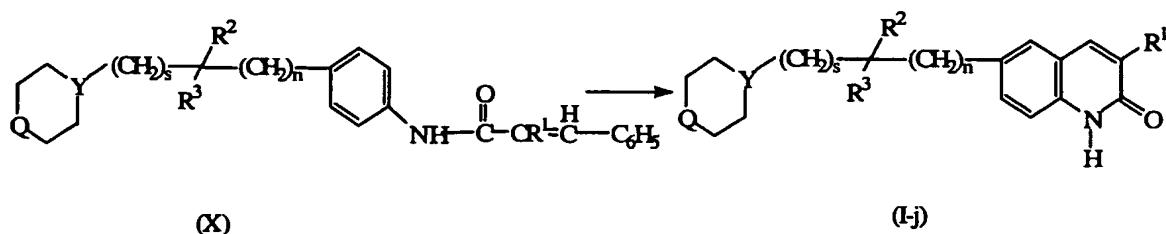
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(VII D)

(I)

b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH herein referred to as compounds of formula (I-j), preferably in the presence of a suitable Lewis Acid, e.g. aluminum chloride either neat or in a suitable solvent such as, for example, an aromatic hydrocarbon, e.g. benzene, chlorobenzene, methylbenzene and the like; halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane and the like; an ether, e.g. tetrahydrofuran, 1,4-dioxane and the like or mixtures of such solvents.

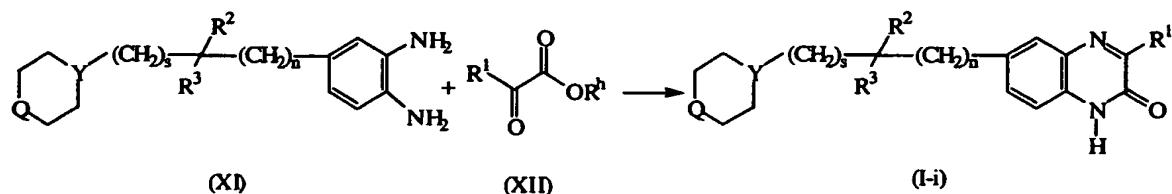


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c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an ester of formula (XII) into compounds of formula (I), wherein X is N and R^2 taken together with R^3 forms $=O$, herein referred to as compounds of formula (I-a-1), in the presence of a carboxylic acid, e.g. acetic acid and the like, a mineral acid such as, for example hydrochloric acid, sulfuric acid, or a sulfonic acid such as, for example, methanesulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid and the like.



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